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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,778	12/03/2007	Hiide Yoshino	2006_1312A	4646

513 7590 07/25/2011

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EXAMINER	
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ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
07/25/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)
	10/588,778	YOSHINO ET AL.
	Examiner	Art Unit
	MARCOS L. SZNAIDMAN	1628

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☒ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 page*.	6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's request for continued examination filed on June 27, 2011.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Status of Claims

Claims 1 and 3-16 are currently pending and are the subject of this office action.

Claims 1 and 3-16 are presently under examination.

Priority

The present application is a 371 of PCT/JP05/001932 filed on 02/09/05, and claims priority to foreign application: JAPAN 2004-032420 filed on 02/09/2004 and JAPAN 2004-032421 filed on 02/09/2004.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a certified English translation of the

foreign application must be submitted in reply to this action. 37 CFR 41.154(b) and 41.202(e).

Failure to provide a certified translation may result in no benefit being accorded for the non-English application.

Information Disclosure Statement

The Information Disclosure Statement filed on June 27, 2011 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment and/or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1 and 3-16 recite 3-methyl-1-phenyl-2-pyrazoline-5-one (edaravone) or a hydrate thereof.

M.P.E.P. #2163 states: "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention....one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process".

The term hydrate corresponds in some undefined way to specifically instantly disclosed chemicals. None of these meet the written description provision of USC 112, first paragraph, due to lack of chemical structural information for what they are since chemical structures are highly variant and encompass a myriad of possibilities. The skilled artisan cannot envision the detailed chemical structure encompassed by hydrates.

Given the broad scope of the subject claimed matter, Applicant has not provided sufficient written description that would allow the skilled artisan to recognize all the hydrates claimed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 8-9 and 13-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 recites: "or about 15 to 240 mg of 3-methyl-1-phenyl-2-pyrazoline-5-one contained in a pharmaceutically acceptable salt of 3-methyl-1-phenyl-2-pyrazoline-5-one or a hydrate of 3-methyl-1-phenyl-2-pyrazoline-5-one or a pharmaceutically acceptable salt as an active ingredient".

It is not understood the meaning of the word "contained" in the above context. It is recommended that Applicant deletes the phrase: "as an active ingredient, or about 15 to 240 mg of 3-methyl-1-phenyl-2-pyrazoline-5-one contained in a pharmaceutically acceptable salt of 3-methyl-1-phenyl-2-pyrazoline-5-one or a hydrate of 3-methyl-1-phenyl-2-pyrazoline-5-one".

Similarly, claim 9 recites: "or about 60 mg of 3-methyl-1-phenyl-2-pyrazoline-5-one contained in a pharmaceutically acceptable salt of 3-methyl-1-phenyl-2-pyrazoline-5-one or a hydrate of 3-methyl-1-phenyl-2-pyrazoline-5-one".

It is not understood the meaning of the word "contained" in the above context. It is recommended that Applicant deletes the phrase: "as an active ingredient, or about 60 mg of 3-methyl-1-phenyl-2-pyrazoline-5-one contained in a pharmaceutically acceptable salt of 3-methyl-1-phenyl-2-pyrazoline-5-one or a hydrate of 3-methyl-1-phenyl-2-pyrazoline-5-one".

Claim 13 recites: "or 3-methyl-1-phenyl-2-pyrazoline-5-one contained in an active ingredient".

Again it is not clear the meaning of the word "contained" in the above context. It is recommended that Applicant deletes the phrase: "or 3-methyl-1-phenyl-2-pyrazoline-5-one contained in an active ingredient".

Claim 14: it is not understood what "equivalent to the intravenous infusion administration" means. Again it is not understood the meaning of "3-methyl-1-phenyl-2-pyrazoline-5-one contained in an active ingredient". Cancellation of Claim 14 is recommended.

Prior Art: counterpart

WO 02/34264 is the PCT counterpart to US 6,933,310.

WO 02/34264 has a 102(b) date as a result of its May 2, 2002 publication date.

US 6,933,310 is prior art under U.S.C 102(e) as a result of its August 23, 2005 publication date.

Because WO 02/34264 and US 6,933,310 appear to have identical disclosures, and because the WO document was published in Japanese language designating the United States, the US Patent US US 6,933,310, which is the National Stage entry of WO 02/34264 is being used as a translation of WO 02/34264 PCT. As such, any reference hereinafter to column and line numbers will be based upon the US Patent, but should be interpreted as referring to the corresponding disclosure of the aforementioned PCT counterpart.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Claims 1, 3-4, 8, and 10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshino et. al. (Neurological Therapeutics (2003) 20:557-564, cited by Applicant, translated from Japanese).

For claims 1 and 3, Yoshino teaches a method of treating Amyotrophic Lateral Sclerosis (ALS) comprising the administration of ederavone (3-methyl-1-phenyl-2-pyrazoline-5-one) (see title for example). Yoshino further teaches the following dose regimen: 14 day administration and then 10 days each month on a long term basis (see page 5, first two lines and page 10, lines 5-9), which means there is at least 1 day holiday period in the administration of ederavone..

For claim 4, Yoshino further teaches the following dose regimen: 20 day administration Monday through Friday (see page 12, lines 6-9), which translates in 5 day administration (Monday through Friday) and 2 day holiday period (Saturday and Sunday).

For claim 8, Yoshino further teaches the administration of 30/mg per day of ederavone (see page 12, last paragraph).

For claim 10, Yoshino further teaches that ederavone was administered once daily (see page 5, first two lines).

For claims 11 and 12, Yoshino further teaches the administration of ederavone by continuous intravenous drip (see page 5, first two lines)

2) Claims 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshino et. al. (Neurological Therapeutics (2003) 20:557-564, cited by Applicant, translated from Japanese) as evidenced by Ikeda (WO 02/34264, cited by Applicant, which is the PCT counterpart to US 6,933,310, see above prior art counterpart, cited in prior office action).

Claims 15 and 16 further limit claim 1, wherein certain symptoms caused by ALS like: decreased respiratory function, voice and speech disorders, dysphagia, or upper and lower extremity motor disorders are being treated. However, the above symptoms are a characteristic of ALS as evidenced by Ikeda and do not further limit the claims. Ikeda teaches that that ALS often begins at middle age, and is a lethal intractable disease, in which the condition rapidly deteriorates from muscular atrophy and muscle weakness to, finally, death due to respiratory insufficiency or the like in a matter of a few years (see column 1, lines 28-34). Ikeda further teaches that ALS is a cryptogenic disease mainly characterized by muscular atrophy and fasciculation. The initial symptoms mainly include hand weakness, dyskinesia in the digits and hands, and fasciculation in the upper limbs, And ALS can be classified into upper limb type, bulbar type, lower limb type and mixed type according to onset site. With any type of the disease, muscle groups of the whole body are impinged with the progress of the symptoms (see column 4, lines 27-38).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 5-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshino et. al. (Neurological Therapeutics (2003) 20:557-564, cited by Applicant, translated from Japanese).

Yoshino teaches all the limitations of claims 5-7 (see 102(b) rejection above), except for the specific dose regimens. However, Yoshino teaches dose regimens like: 1- 14 day administration and then 10 days each month on a long term basis (see page 5, first two lines and page 10, lines 5-9), which means there is at least 1 day holiday period in the administration of ederavone, or 2- 20 day administration Monday through Friday (see page 12, lines 6-9), which translates in 5 day administration (Monday through Friday) and 2 day holiday period (Saturday and Sunday). These dose regimens are very close and/or overlap with the dose regimens of claims 5-7.

MPEP 2144.05 states: In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim,* 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990. MPEP 2144.05 further states: "A *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773

(Fed. Cir. 1985) (Court held as proper a rejection of a claim directed to an alloy of "having 0.8% nickel, 0.3% molybdenum, up to 0.1% iron, balance titanium" as obvious over a reference disclosing alloys of 0.75% nickel, 0.25% molybdenum, balance titanium and 0.94% nickel, 0.31% molybdenum, balance titanium.)." Thus resulting in the practice of claims 5-7 with a reasonable expectation of success.

Yoshino teaches all the limitations of claim 9 (see 102(b) rejection above), except for the specific administration of 60 mg of ederavone. However, Yoshino teaches the administration of 30 mg/day of ederavone (see page 12, last paragraph) which is close to the amount claimed.

.MPEP 2144.05 states: "A *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (Court held as proper a rejection of a claim directed to an alloy of "having 0.8% nickel, 0.3% molybdenum, up to 0.1% iron, balance titanium" as obvious over a reference disclosing alloys of 0.75% nickel, 0.25% molybdenum, balance titanium and 0.94% nickel, 0.31% molybdenum, balance titanium.)." Thus resulting in the practice of claim 9 with a reasonable expectation of success.

2) Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshino et. al. (Neurological Therapeutics (2003) 20:557-564, cited by Applicant,

translated from Japanese) in view of Ikeda (WO 02/34264, cited by Applicant, which is the PCT counterpart to US 6,933,310, see above prior art counterpart, cited in prior office action).

Yoshino teaches all the limitations of claims 13-14 (see 102(b) rejection above), except for the specific rate of administration of ederavone. However, Ikeda teaches a method of treating ALS comprising the administration of ederavone (see for example claims 1-5). Ikeda further teaches that: the dose of the medicament can be selected according to various conditions including type of disease being treated, progress of the disease or degree of the symptoms, and age and weight of the patient. In general approximately 0.01 microgram/kg to 10 mg/kg per day for an adult is administered by injection or drip (see column 5, lines 52-63). These dose regimens are very close and/or overlap with the dose regimens of claims 13 and 14.

MPEP 2144.05 states: In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim,* 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990. MPEP 2144.05 further states: "A *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (Court held as proper a rejection of a claim directed to an alloy of "having 0.8% nickel, 0.3% molybdenum, up to 0.1% iron, balance titanium" as obvious

over a reference disclosing alloys of 0.75% nickel, 0.25% molybdenum, balance titanium and 0.94% nickel, 0.31% molybdenum, balance titanium.)." Thus resulting in the practice of claims 13-14 with a reasonable expectation of success.

Conclusion

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1628.
July 13, 2011